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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,440	02/05/2004	Michal Daniely	26003	3178

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EXAMINER

DUFFY, BRADLEY

ART UNIT	PAPER NUMBER
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1643

MAIL DATE	DELIVERY MODE
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08/10/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/771,440

Applicant(s)

DANIELY ET AL.

Examiner

Brad Duffy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37, 39-55 and 57-73 is/are pending in the application.
- 4a) Of the above claim(s) 1-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 37, 39-55 and 57-73 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application
- ☒ Other: Exhibit A

DETAILED ACTION

1. The amendment filed May 15, 2007, is acknowledged and has been entered. Claims 38 and 56 has been cancelled. Claims 37, 41-53, 55 and 58-71 have been amended. Claims 72-73 have been newly added
2. Claims 1-37, 39-55 and 57-73 are pending in the application.
3. Claims 1-36 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. As Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement in the reply filed on October 17, 2006, the election has been treated as an election without traverse (MPEP § 818.03(a).
4. Claims 37, 39-55 and 57-73 are under examination.
5. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

Priority

6. Applicant's claim under 35 USC §§ 119 and/or 120 for benefit of the earlier filing date of the U.S. Provisional Application No. 60/459,992, filed April 4, 2003, is acknowledged.

However, claims 37, 39-55 and 57-73 do not properly benefit from the earlier filing because, for example, the instant claims recite the limitation "at least two stains", which is interpreted as two or more stains and support for using more than two stains was not found in U.S. Provisional Application No. 60/459,992.

Furthermore, the claims do not properly benefit under §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since the claims are

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rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). See M.P.E.P. § 201.11.

Accordingly, the effective filing date of the claims is deemed the filing date of the instant application, namely February 5, 2004.

Grounds of Objection and Rejection Withdrawn

7. Unless specifically reiterated below, Applicant's amendment and/or arguments filed May 15, 2007, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed December 27, 2006.

Response to the Declaration under 37 C.F.R. § 1.132

8. The declaration under 37 C.F.R. § 1.132 filed April 24, 2007 is insufficient to overcome the rejection of claims 37-48, 51-65 and 68-71 under 35 U.S.C. 102(a) as being anticipated by Daniely et al (Annales de Genetique, 46:153, September 2003), as evidenced by Shimoni et al. [Leukemia, 16:1413-1418, August 2002], Skacel et al. (Anal. Quant. Cytol. Histol. 23(6): 381-387, December 2001], and the rejection of claims 37, 49-50, 55 and 66-67 under 35 U.S.C. 103(a) as being unpatentable over Daniely et al. (Annals de Genetique, 46:153, September 2003) in view of US Patent 6,418,236 (Ellis et al., July 9, 2002), as set forth in the last Office action, for the following reasons:

In this case, the declaration states:

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We, Michal Daniely of 5 Harimon Street, 55900 Ganei Tikva, Israel; Tal Kaplan of 4/3 HaMagal Street, 70800 Gan-Yavne, Israel; Eran Kaplan of 3 Paldi Street, 76248 Rechovot, Israel; and Avner Freiburger of 19b Emek Dotan Street, 44621 Kfar-Saba, Israel; declare as follows:

1. We are the only inventors of the invention disclosed and claimed in the above-identified application; and

2. That the co-authors, Ronni Rona, Sylvia Lev, Yulia Zilberstein, Dvora Kidron D, and Ilan Leibovitch identified in a poster entitled "Combined analysis of morphology and FISH for the monitoring of bladder cancer", published on September 2003 in *Annales de Genetique*, 46:153, were identified as co-authors on said poster for their collaborative efforts operating under our guidance and direction, and were not co-inventors of the above-identified application.

Notably, the declaration submitted on May 15, 2007, identifies the prior art entitled "Combined analysis of morphology and FISH for the monitoring of bladder cancer" as a poster abstract. In this case, the journal, *Annales de Genetique* published in September 2003 the Program and abstracts from the FECC conference that also occurred in September 2003; and this Program indicates that the poster abstract entitled "Combined analysis of morphology and FISH for the monitoring of bladder cancer" was presented as an "Oral Communication" at the FECC conference. (see attached Exhibit A, item 3.4, which discloses that this poster abstract was presented as an "Oral Communication").

Therefore, as there is evidence that the contents of Daniely et al (*Annales de Genetique*, 46:153, September 2003) was publicly disclosed to others in the public without limitation, restriction or obligation of secrecy to the inventor during this conference, as a printed poster abstract and presented orally, the disclosure of Daniely et al still qualifies as prior art under 35 U.S.C. 102(a) and 35 U.S.C. 103(a).

Notably, MPEP § 2132 states, in part, that:

The term "others" in 35 U.S.C. 102(a) refers to any entity which is different from the inventive entity. The entity need only differ by one person to be "by others." This holds true for all types of references eligible as prior art under 35 U.S.C. 102(a) including publications, as well as public knowledge and use.

Accordingly, although the merit of the declaration under 37 C.F.R. § 1.132 has been carefully considered, Applicant's declaration and the abstract cited as

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prior art as the basis of the rejection of the claims under § 102(a) provide factual evidence that the detailed results, which were presented at the conference held September 2003, was disseminated in written format to others in the public without limitation, restriction or obligation of secrecy to the inventor.

The statutory phrase "printed publication" has been interpreted to mean that, before the critical date, the reference must have been sufficiently accessible to the public interested in the art; dissemination and public accessibility are the keys to the legal determination whether a prior art reference was "published". *In re Hall*, 288 USPQ 453, 455 (Fed. Cir. 1986). Moreover, the term "printed publication" has been defined as a work that is "disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it and recognize and comprehend therefrom the essentials of the claimed invention without need of further research or experimentation". *In re Wyer*, 210 USPQ 790, 794 (CCPA 1981). See also *Constant v. Advanced Micro-Devices Inc.* 7 USPQ2d 1057, 1062 (CAFC 1988).

It is submitted that the poster must have been sufficiently accessible to the public interested in the art, namely the attendees of the conference at which the poster was presented; and it is further noted that compilations of abstracts of the posters and oral presentations to be presented at such conferences are routinely made available to attendees in advance of their presentation. The publication requirement may also be satisfied by distributing or making the paper available at a conference where persons interested or skilled in the subject matter of the paper were told of the paper's existence and informed of the its contents. *Massachusetts Institute of Technology v. AB Fortia*, 227 USPQ 428, 432 (Fed. Cir. 1985).

It is acknowledged, however, that a reference must describe an invention sufficiently "to have placed the public in possession of it". *In re Donohue*, 266 USPQ 619, 621 (Fed. Cir. 1985). Still, the standard for what makes a disclosure enabling is that "one of ordinary skill in the art could have combined the

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publication's description of the invention with his own knowledge to make the claimed invention". *Id.* In this instance, given the routine practice of dissemination of information at scientific meetings, it is submitted in the absence of evidence to the contrary that one of ordinary skill in the art, given benefit of the information disseminated, could have combined that description of the invention with his or her own knowledge to make and use the claimed invention.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. The rejection of claims 37, 39-55 and 57-73 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

At page 19 of the amendment filed May 15, 2007, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereafter "Guidelines"). A copy of this publication can be

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viewed or acquired on the Internet at the following address:

<http://www.gpoaccess.gov/>.

In this instance, the claims 37, 39-55 and 57-73 are directed to a broad genus of methods of identifying transitional cell carcinoma cells or diagnosing bladder cancer using staining methods that require the use of at least two members of a genus of "stains". Some of the claims are further directed to using methods that use stains, which are "morphological stains", "immunological stains", "cytogenetical stains", "*in situ* hybridization stains" or "DNA stains". According to the disclosure and/or claims, the morphological stains include a May-Grunwald-Giemsa stain, a Giemsa stain, a Papanicolau stain, a Hematoxylin-Eosin stain, and a DAPI stain. The immunological stains include fluorescently labeled immunohistochemistry stains, radiolabeled immunohistochemistry stains, and immunocytochemistry stains. The activity stains include cytochemical stains, and substrate binding assay stains. The cytogenetical stains include G-banding stains, R-banding stains, Q-banding stains, and C-banding stains. The *in situ* hybridization stains include fluorescent *in situ* hybridization stains, radiolabeled *in situ* hybridization stains, digoxigenin labeled *in situ* hybridization stains, and biotinylated *in situ* hybridization stains. The DNA stains include DNA-binding fluorescent dyes.

However, as will be explained in further detail in the following paragraphs, the specification does not describe the structure of a sufficient number of species of the genus of "stains" used by these methods, or a sufficient number of species of any of the subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, *in situ* hybridization stains or DNA stains to reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Applicant has remarked at page 20 of the response filed May 15, 2007 that "claims 37, 41-53, 55 and 58-70 have been amended to recite "staining method" instead of "stain". Accordingly, Applicant has argued at page 19 that these staining methods have adequate written support at e.g., pages 11-14 of the

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instant application as these staining methods are well-known in the art. Therefore, Applicant has submitted that the specification, as filed, adequately describes the claimed invention, (i.e., the staining methods and stains used to identify transitional cell carcinoma in a urine sample).

Contrary to Applicant's argument, however, the claimed methods still required the use of a structurally and functionally diverse genus of "stains", or a subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains or DNA stains that have not been adequately described in the specification as filed. Notably, as evidenced by Conn's Biological Stains, 10th Edition (edited by Horobin et al, May 2002) at page 8 of the Office action mailed December 27, 2006, one of skill in the art could not predict the structure of a stain given its function or the function of a stain given its structure. Therefore, one of skill in the art would not immediately envision or recognize the genus of stains and the subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains and DNA stains that could be used in the claimed methods as the members do not all do not share common structural features that relate to their stated functions. In the response filed May 15, 2007, Applicant has provided some examples of staining methods and some stains used in these staining methods that may be included in the genus of stains and or subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains or DNA stains but has not provided any evidence that these stains share structural features that relate to their stated function that would allow one of skill in the art to immediately envision or recognize the members of the genus of stains and or subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains or DNA stains from any other that could be used in the claimed methods. Accordingly the genus of stains and the subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains and DNA stains that can be used in the claimed the staining methods to

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identify transitional cell carcinoma in a urine sample have not been adequately described by these examples, or by the specification as filed.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568). In this instance, while the specification describes the structure of some stains that may be considered morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains or DNA stains, these stains do not share a common structure and as evidenced by Conn's Biological Stains (*supra*), one cannot predict the structure of a stain from a given function and vice versa.

"[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). Here, there is no language that adequately describes the genus of stains to which the claims are directed, or the subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains or DNA stains.

Again, the genus of stains and the subgenera of morphological stains, immunological stains, activity stains, cytogenetical stains, in situ hybridization stains and DNA stains all do not share common structural features that relate to their stated functions.

What structural and/or functional features define members of the genus of "morphological stains"? How are such stains structurally and/or functionally distinct from, for example, members of the genus of "activity stains"? How does one "stain" an activity? How are "cytogenetical stains" different from "DNA stains"?

Given the lack of particularity with which the "stains" to which the claims are directed are described in the specification, it is submitted that the skilled

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artisan could not immediately envision, recognize or distinguish at least most of the members of the genus of "stains" or the subgenera of "morphological stains", "immunological stains", "activity stains", "cytogenetical stains", "in situ hybridization stains" and "DNA stains" to which the claims are directed; and therefore the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. The rejection of claims 37, 39-48, 51-55, 57-65 and 68-73 under 35 U.S.C. 102(a), as being anticipated by Daniely et al (of record), as evidenced by Shimoni et al (of record) and Skacel et al (of record), is maintained.

At page 20 of the amendment filed May 15, 2007, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that the instant application is entitled to a priority of April 4, 2003, as the instant applicant claims priority to U.S. Provisional Application No. 60/459,992, and therefore Daniely et al is not available as prior art.

In response, it is noted that support for using more than two stains was not found in U.S. Provisional Application No. 60/459,992 and Applicant has not supplied any evidence that the priority application supports using more than two

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stains. Additionally, the claims are rejected herein under 35 U.S.C. § 112, first paragraph. Therefore, as noted above, the priority date of the instant claims is February 5, 2004; and accordingly Daniely et al is available as prior art under § 102(a).

Furthermore, Applicant has submitted that the declaration filed under 37 C.F.R. § 1.132 is sufficient to overcome this rejection. However, as set forth hereinabove, the declaration is insufficient to overcome the rejection in this case as there is evidence that the disclosure of Daniely et al was present publicly as an oral communication (see attached exhibit A). In addition, Applicant's declaration and the abstract cited as prior art as the basis of the rejection of the claims under § 102(a) provide factual evidence that the detailed results, which were presented at the FECC conference held September 2003, was disseminated in written format to the public without limitation, restriction or obligation of secrecy to the inventor; and therefore, the disclosure of Daniely et al is still deemed available as prior art under § 102(a).

Furthermore, as evidenced by Shimoni et al, the BIOVIEW DUET system is an automated microscope capable of dual imaging and one method of using the BIOVIEW DUET system comprises a) staining the cells, b) imaging the stained cells, c) staining the cells again with a different stain) d) imaging the second stain and then e) simultaneously viewing said stained cells. (see entire document, e.g., page 1413, second column).

For these reasons, the Examiner disagrees with Applicant's contention that the rejection has been overcome and the rejection of claims 37, 39-48, 51-55, 57-65 and 68-73 under 35 U.S.C. 102(a) as being anticipated by Daniely et al (of record), as evidenced by Shimoni et al (of record) and Skacel et al (of record), is maintained.

13. The rejection of claims 37, 39-48, 52-53, 55, 57-65 and 69-70 are under 35 U.S.C. 102(b), as being anticipated by Skacel et al (of record), is maintained.

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At page 21 of the amendment filed May 15, 2007, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that Skacel et al do not anticipate the claims as they teach imaging the cells under one imaging mode.

In response, it is noted that while Skacel et al teach using a fluorescence microscope to image both DAPI and FISH stains, both the specification and the commonly known definition of "imaging mode" in the microscopy art support that imaging a DAPI stain requires a different imaging mode than the imaging mode used to image a particular FISH stain as each stain emits light at a different wavelength.

Notably, support for this interpretation occurs in the specification at page 5, lines 7-8, which teaches that imaging modes can be specific to a stain and at page 11, lines 30-31 that discloses appropriate filters are required to visualize different stains. Therefore, while Skacel et al teach using the same fluorescent microscope to image the cells, Skacel et al are deemed to teach imaging said cells by two different imaging modes, i.e. a DAPI imaging mode and a FISH imaging mode.

For these reasons, the Examiner disagrees with Applicant's contention that the rejection has been overcome and the rejection of claims 3737, 39-48, 52-53, 55, 57-65 and 69-70 under 35 U.S.C. 102(a) as being anticipated by Skacel et al (of record) is maintained.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. The rejection of claims 37, 54, 55 and 71-73 under 35 U.S.C. 103(a) as being unpatentable over Skacel et al (of record), in view of Daniely et al (of record), is maintained.

At page 22 of the amendment filed May 15, 2007, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that the instant application is entitled to a priority of April 4, 2003 as the instant applicant claims priority to U.S. Provisional

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Application No. 60/459,992 and therefore, Daniely et al is not available as prior art.

In response, it is noted that support for using more than two stains was not found in U.S. Provisional Application No. 60/459,992 and Applicant has not supplied any evidence that the priority application supports using more than two stains. Therefore, the priority date of the instant claims is February 5, 2004 and Daniely et al is available as prior art.

For these reasons, the Examiner disagrees with Applicant's contention that the rejection has been overcome and the rejection of claims 37, 54, 55 and 71-73 under 35 U.S.C. 103(a) as being unpatentable over Skacel et al (of record), in view of Daniely et al (of record) is maintained.

17. The rejection of claims 37, 49-51, 54-55, 66-68 and 71 under 35 U.S.C. 103(a) as being unpatentable over Skacel et al (of record) in view of US Patent No. 6,418,236 (of record), is maintained.

At page 22 of the amendment filed May 15, 2007, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that US Patent No. 6,418,236 does not teach the limitation of imaging the same cells as US Patent 6,418,236 only discloses a method of analyzing a biological specimen that has been consecutively stained with hematoxylin-eosin (H/E) and immunohistochemistry (IHC) or in situ hybridization (ISH) methods on parallel (i.e., different) tissue sections (Column 1, lines 60-65 of US Patent No. 6,418,236).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

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Furthermore, as explained in the preceding Office action US Patent 6,418,236 teaches image analysis using a microscope capable of dual imaging to image cells stained with two stains with at least one stain being an immunological stain (immunohistochemistry stain) or an activity stain (cytochemical stain). (see entire document, e.g., column 1, lines 26-59, column 4, lines 31-37, column 5, lines 1-15). Notably, the parallel imaging technique is only disclosed as one particular embodiment at column 1, line 65. However, at column 1, lines 56-59, US Patent 6,418,236 discloses that the microscope is capable of dual imaging to determine if the same cells are stained with two stains of interest.

Therefore as explained in the previous office action, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to identify transitional cell carcinoma cells or diagnose bladder cancer from a urine sample, by staining nucleated cells of a urine sample with at least two stains as taught in Skacel, wherein at least one stain of the two stains is an immunological stain, an activity stain or a cytogenetical stain and imaging the stained cells with the automated microscope capable of dual imaging as taught by US Patent 6,418,236 to identify transitional cell carcinoma cells or diagnose bladder cancer.

For these reasons, the Examiner disagrees with Applicant's contention that the burden of showing a *prima facie* case of obviousness was not met by the first Office action on the merits and the rejection of claims 37, 49-51, 54-55, 66-68 and 71 under 35 U.S.C. 103(a), as being unpatentable over Skacel et al (of record) in view of US Patent No. 6,418,236 (of record), is maintained.

18. The rejection of claims 37, 49-50, 55, and 66-67 under 35 U.S.C. 103(a), as being unpatentable over Daniely et al (of record) in view of US Patent 6,418,236 (of record), is maintained.

At page 23 of the amendment filed May 15, 2007, Applicant has traversed this ground of rejection.

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Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that the instant application is entitled to a priority of April 4, 2003 as the instant applicant claims priority to U.S. Provisional Application No. 60/459,992 and therefore, Daniely et al is not available as prior art.

In response, it is noted that support for using more than two stains was not found in U.S. Provisional Application No. 60/459,992 and Applicant has not supplied any evidence that the priority application supports using more than two stains. Additionally, the claims are rejected herein under 35 U.S.C. § 112, first paragraph. Therefore, the effective filing date of the instant claims is February 5, 2004; and accordingly Daniely et al is available as prior art.

For these reasons, the Examiner disagrees with Applicant's contention that the rejection has been overcome and the rejection of claims 37, 49-50, 55, and 66-67 under 35 U.S.C. 103(a), as being unpatentable over Daniely et al (of record) in view of US Patent 6,418,236 (of record), is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 37, 39-55 and 57-71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

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Claims 37, 39-55 and 57-71 have been amended to recite, "imaging said stained nucleated cells by at least two imaging modes, wherein one imaging mode of said at least two imaging modes being different from another imaging mode of said at least two imaging modes", as opposed to "exposing said stained nucleated cells to at least two imaging modes".

Applicant has indicated that support for this amendment can be found for example, on Page 10, lines 30-33 and Page 11, lines 1-19.

Contrary to Applicant's assertion, however, it does not appear that the specification, including the claims, as originally filed, provides written support for the language of the claims.

Notably, in the response filed May 15, 2007, at page 21, 2nd paragraph, Applicant has asserted that "one imaging mode" includes visualizing DAPI and FISH stains with dark modality using a fluorescence microscope, and therefore argues that the specific disclosure at pages 10 to 11 of the specification supports that different imaging modes require the use of a different microscope, i.e., a light microscope; however, the disclosure at pages 10 to 11 does not limit imaging modes in any way and the specification teaches at, for example, page 5, lines 7-8, that imaging modes can be specific to each stain. Furthermore, it is well-known in the art that while DAPI and FISH stains may both be visualized with dark modality using a fluorescence microscope, that each particular stain emits a distinct wavelength and therefore would be considered to be imaged by a different imaging mode using the same fluorescence microscope. Notably, at page 11, lines 30-31 the specification discloses that appropriate filters are required to visualize the stains and in using a different filter or visualizing a different stain discloses that each stain can be imaged by a different imaging mode.

In this instance, as noted above, Applicant has amended the claims to recite "imaging said stained nucleated cells by at least two imaging modes, wherein one imaging mode of said at least two imaging modes being different from another imaging mode of said at least two imaging modes", as opposed to

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"exposing said stained nucleated cells to at least two imaging modes", with the intent of obviating the stated ground of rejection under 35 USC § 102 and 35 USC § 103.

Yet, as also noted above, both the art and the specification teach that a DAPI imaging mode and a FISH imaging mode would be considered to be different imaging modes and that dark modality using a fluorescent microscope is therefore inclusive of multiple different imaging modes.

So, to the extent that the amendment attempts to redefine the concept of "imaging modes", it appears that the claims are not supported by the specification as originally filed. Therefore, it is submitted that this clearly illustrates that such amendments have in fact introduced new concepts.

Conclusion

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21. No claim is allowed.

22. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

23. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Halling et al (Journal of Urology, 164:1768-1775, November 2000) discloses a method of identifying transitional cell carcinoma cells and diagnosing bladder cancer in cells stained with DAPI and FISH stains. Bubendorf et al (Anatomic Pathology, 116:79-86, 2001) discloses a method of identifying transitional cell carcinoma cells and diagnosing bladder cancer in cells stained with DAPI and FISH stains. Darzynkiewicz et al (Experimental Cell Research, 249:1-12, 1999) discloses an automated cell-imaging device capable of dual imaging.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM with alternate Fridays off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

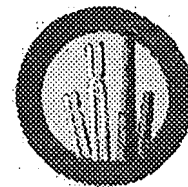
Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner, Art Unit 1643

bd
August 5, 2007



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